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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/676,135	09/29/2000	Bryan J. Boyle	21272-034	9596

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HYSEQ, INC.
670 Almanor Avenue
Sunnyvale, CA 94085

EXAMINER
SOUAYA, JEHANNE E

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 10/22/2002 14

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/676,135	Boyle et al.
Examiner	**Art Unit**
Jehanne Souaya	1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☐ Responsive to communication(s) filed on _____.

2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *10, 11, 24, 25, 29, and 31* is/are pending in the application.

4a) Of the above, claim(s) *24 and 29* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *10, 11, 25, and 31* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *11, 12*
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Currently, claims 10, 11, 25, and newly added claim 31 are under consideration in the instant application. All the amendments and arguments have been thoroughly reviewed but are deemed insufficient to place this application in condition for allowance. Any rejections not reiterated are hereby withdrawn. The following rejections are either newly applied or are reiterated. They constitute the complete set being presently applied to the instant Application. Response to Applicant's arguments follow. This action is FINAL.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior office action.

3. The rejections under 35 USC 112/first paragraph, written description, over claims 12 and 13, and 35 USC 102(a) over claim 13, made in the previous office action, are moot as claims 12 and 13 have been canceled.

Maintained Rejections

Claim Rejections - 35 USC § 101

4. Claims 10, 11, 25, and newly added claim 31 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility.

The claims encompass isolated polypeptides that are at least 99 % identical to SEQ ID NOS 4. The claims further encompass the mature protein of SEQ ID NO 4. The specification defines "mature protein coding region" (p. 19) as a polypeptide lacking a signal sequence. Since the specification teaches that amino acids 1-20 of SEQ ID NO 4 are drawn to a signal peptide, the recitation of "mature protein thereof" in claim 10 is interpreted to mean a polypeptide comprising amino acids 21-374 of SEQ ID NO 4.

The specification teaches that SEQ ID NO 4 is predicted to be encoded by the nucleic acid of SEQ ID NO 3, and that a signal peptide is predicted to be encoded by amino acids 1-20 of SEQ ID NO 4. The specification further teaches that a predicted fifteen residue GPI anchor exists at amino acids 360-374 of SEQ ID NO 4, and that predicted zinc binding regions as well as predicted carboxypeptidase A metalloprotease (M14) family signature domains were found throughout SEQ ID NO 4 (p.4). The specification, however, does not demonstrate the biological activity or function of SEQ ID NOS 4 or where "active domains" are located. Such a demonstration is critical for the artisan to know how to use SEQ ID NO 4 as carboxypeptidases that belong to the GPI anchor class, such as carboxypeptidase M, have different biological activity and substrate specificity (cleave basic amino acids and are involved in processing of peptide hormones) than that of carboxypeptidase A (cleaves hydrophobic amino acids from peptides in the gut– see Reznik and Fricker, Cell. Mol. Life Sci, 2001, pp 1790-1804, vol. 58, figure 1). The specification asserts that the signal peptide, has use on its own, but teaches that

this use (which is not disclosed in the specification) must be confirmed by expression in mammalian cells and sequencing of the cleaved product.

Metallocarboxypeptidases are generally known to be involved in cleavage of peptides, however a large class of Metallocarboxypeptidases exist which have zinc binding regions and also have a wide range of functions (see Vendrell et al, Biochimica et Biophysica Acta; 2000; vol. 177, pp 284-298), therefore the prediction of a putative GPI anchor region as well as zinc binding regions and putative carboxypeptidase A metalloprotease (M14) family signature domains in SEQ ID NO 4 would not indicate to one of skill a specific or substantial utility for the claimed polypeptides. Further, the specifications disclosure of a specific or substantial utility for the claimed polypeptide is unclear as the specification teaches that SEQ ID NO 4 also has homology to carboxypeptidase B, whose biological activity and function is different than that of carboxypeptidase A. It is further noted that the specification asserts at page 11, that SEQ ID NO 4 is expected to have either secreted metallocarboxypeptidase like activity (it is noted that Carboxypeptidase A and B, while having different functions, are considered part of the family of secreted carboxypeptidases) or GPI anchored metallocarboxypeptide like activity (it is noted that such carboxypeptidases belong to a different class of carboxypeptidases than that of carboxypeptidase A or B, which have different biological activities and functions than the latter, see Vendrell et al). Thus, given such conflicting teachings in the specification, one of skill would not know how to use the polypeptide of SEQ ID NO 4.

The specification asserts the following uses for the claimed polypeptides: at page 49, the specification teaches that the polypeptides can be used a) to generate an antibody that specifically binds the polypeptide, b) as molecular weight markers, and c) as food supplements. The specification further asserts that the claimed polypeptides can be used as potential therapeutics in digestive disorders, autoimmunity, inflammatory disorders and Alzheimer's disease (p. 14). At page 49, the specification teaches that the polypeptides can also be used in assays to determine biological activity or levels of protein in biological fluids, and also to isolate correlative receptors or ligands. The claimed polypeptides, however, are not supported by a specific asserted utility because the disclosed uses of the polypeptides are not specific and are generally applicable to any polypeptide. These are non-specific uses that are applicable to polypeptides in general and not particular or specific to the polypeptide being claimed.

Further, the claimed polypeptides are not supported by a substantial utility because no substantial utility has been established for the claimed subject matter. For example, a polypeptide can be used to obtain an antibody. The antibody could then be used in conducting research to isolate the protein. The need for such research clearly indicates that the protein and/or its function is not disclosed as to a currently available or substantial utility. A starting material that can only be used to produce a final product does not have substantial asserted utility in those instances where the final product is not supported by a specific and substantial utility. In this case, none of the antibodies that are to be produced as final products resulting from processes involving the claimed polypeptides have specific and substantial utilities. The research contemplated by

applicant(s) to characterize potential protein products, especially their biological activities, does not constitute a specific and substantial utility. Identifying and studying the properties of a protein itself or the mechanisms in which the protein is involved does not define a "real world" context of use. Similarly, the other listed and asserted utilities as summarized above or in the instant specification are neither substantial nor specific due to being generic in nature and applicable to a myriad of such compounds. Note, because the claimed invention is not supported by a specific and substantial asserted utility for the reasons set forth above, credibility of the utility has not been assessed.

It is noted that the specification teaches that SEQ ID NO 4 has about 46% identity to Bothrops jararaca carboxypeptidase homologue and 48% identity to mutant carboxypeptidase B. Neither the specification, nor the art teach the activity or biological function of Bothrops japonica carboxypeptidase homologue. Further, the art teaches the pitfall of using homology to assign protein function. Bork (TIG, vol. 12, pp 425-427) teaches that a single wrongly annotated entry will lead to whole families with artificial functions based on similarities to that entry (see p. 426, col 1) and that similarities might only be restricted to certain domains, but the function is transferred to a whole protein(col. 3). With respect to the % identity to carboxypeptidase B mutant, a sequence search revealed that SEQ ID NO 4 also has 39.6 % identity to bovine carboxypeptidase B (cleaves basic amino acids) as well as 38.1% identity to mouse carboxypeptidase A (cleaves hydrophobic amino acids). Further, Reznik teaches that carboxypeptidases which have different functions, but belong to the same subfamily, only have

about 50% homology to each other. Therefore, absent any evidence as to the actual function or activity of the polypeptide of SEQ ID NO 4, one skilled in the art would not know whether the biochemical activity of the claimed subject matter would be the same as that of a similar known biomolecule. Further, with respect to newly added claim 31 which is drawn to a polypeptide having 99 % identity to SEQ ID NO 4, it is known for nucleic acids as well as proteins, that even a single nucleotide or amino acid change or mutation can destroy the function of the biomolecule in many instances, albeit not in all cases. The effects of these changes are largely unpredictable as to which ones have a significant effect versus not. (See Proudfoot et al, J. Biol. Chem., vol. 271 pp. 2599-2603 which teaches that in recombinant human RANTAS, a single residue at the amino terminus of the molecule can change the activity of the polypeptide, see abstract). The specification does not teach the biological function or activity of SEQ ID NO:4. Therefore, the citation of sequence similarity results in an unpredictable and therefore unreliable correspondence between the claimed biomolecule and the indicated similar biomolecule and therefore lacks support regarding utility. Further experimentation would be required of the skilled artisan to determine a use for the polypeptides of the claimed invention. As noted by Brenner v. Manson, 383 US 519, 535-536 (1996), "Congress intended that no patents be granted on a chemical compound whose sole "utility" consists of its potential role as an object of use - testing... a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion."

New Grounds of Rejection

Claim Rejections - 35 USC § 112

5. Claims 10, 11, 25 and newly added claim 31 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Specifically, since the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to make or use the claimed invention.

There are many factors to be considered when determining whether there is sufficient evidence to support determination that a disclosure does not satisfy the enablement requirements and whether any necessary experimentation is undue (See In re Wands, 858 F. 2d 731, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). These factors include, but are not limited to:

Quantity of Experimentation Necessary
Amount of Direction and Guidance
Presence and Absence of Working Examples
Nature of the Invention
Level of predictability and unpredictability in the art

The following rejection contains new grounds of rejection with respect to newly added claim 31, necessitated by the amendment filed 8/7/2002.

It is noted that given the disclosure of the sequence of SEQ ID NO 4 in the specification, one of skill in the art would be enabled to make the polypeptide of SEQ ID NO 4. The skilled artisan, however, would not be enabled to use the polypeptide of SEQ ID NO 4, kits or compositions comprising such, nor would the skilled artisan be enabled for making or using variants or homologs of SEQ ID NO 4.

The claimed invention is drawn to a polypeptide of SEQ 4, or the mature protein thereof. With regard to the mature protein of SEQ ID NO 4, absent a teaching of a specific amino acid sequence that is "the mature protein" of SEQ ID NO 4, the examiner assumes that such is drawn to amino acids 21-364 of SEQ ID NO 4 as the specification defines "mature protein coding region" at p. 19 to be a polypeptide without a signal sequence and the specification also teaches that amino acids 1-20 of SEQ ID NO 4 correspond to a signal peptide.

The specification teaches the sequence of SEQ ID NO 4. The specification, however, does not teach one of skill in the art how to use the polypeptide of SEQ ID NO 4, nor the mature protein of SEQ ID NO 4 (amino acids 21-364 of SEQ ID NO 4). The specification teaches that SEQ ID NO 4 is predicted to be encoded by the nucleic acid of SEQ ID NO 3, and that a signal peptide is predicted to be encoded by amino acids 1-20 of SEQ ID NO 4. The specification further teaches that a predicted fifteen residue GPI anchor exists at amino acids 360-374 of SEQ ID NO 4, and that predicted zinc binding regions as well as predicted carboxypeptidase A metalloprotease (M14) family signature domains were found throughout SEQ ID NO 4 (p.4). The specification, however, does not demonstrate the biological activity or function of SEQ ID

NOS 4 or where "active domains" are located. Such a demonstration is critical for the skilled artisan to know how to use SEQ ID NO 4 as carboxypeptidases that belong to the GPI anchor class, such as carboxypeptidase M, have different biological activity and substrate specificity (cleave basic amino acids and are involved in processing of peptide hormones) than that of carboxypeptidase A (cleaves hydrophobic amino acids from peptides in the gut– see Reznik and Fricker, Cell. Mol. Life Sci, 2001, pp 1790-1804, vol. 58, figure 1). The specification asserts that the signal peptide, has use on its own, but teaches that this use (which is not disclosed in the specification) must be confirmed by expression in mammalian cells and sequencing of the cleaved product.

Metallocarboxypeptidases are generally known to be involved in cleavage of peptides, however a large class of metallocarboxypeptidases exist which have zinc binding regions and also have a wide range of functions (see Vendrell et al, Biochimica et Biophysica Acta; 2000; vol. 177, pp 284-298), therefore the prediction of a putative GPI anchor region as well as zinc binding regions and putative carboxypeptidase A metalloprotease (M14) family signature domains in SEQ ID NO 4 would not indicate to one of skill a specific or substantial utility for the claimed polypeptides. Further, the specifications disclosure of a specific or substantial utility for the claimed polypeptide is unclear as the specification teaches that SEQ ID NO 4 also has homology to carboxypeptidase B, whose biological activity and function is different than that of carboxypeptidase A. It is further noted that the specification asserts at page 11, that SEQ ID NO 4 is expected to have either secreted metallocarboxypeptidase like activity (it is noted that

Carboxypeptidase A and B, while having different functions, are considered part of the family of secreted carboxypeptidases) or GPI anchored metallocarboxypeptide like activity (it is noted that such carboxypeptidases belong to a different class of carboxypeptidases than that of carboxypeptidase A or B, which have different biological activities and functions than the latter, see Vendrell et al). Thus, given such conflicting teachings in the specification, one of skill would not know how to use the polypeptide of SEQ ID NO 4.

It is noted that the specification teaches that SEQ ID NO 4 has about 46% identity to Bothrops jararaca carboxypeptidase homolog and 48% identity to mutant carboxypeptidase B. Neither the specification, nor the art teach the activity or biological function of Bothrops japonica carboxypeptidase homolog. Further, the art teaches the pitfall of using homology to assign protein function. Bork (TIG, vol. 12, pp 425-427) teaches that a single wrongly annotated entry will lead to whole families with artificial functions based on similarities to that entry (see p. 426, col 1) and that similarities might only be restricted to certain domains, but the function is transferred to a whole protein(col. 3). With respect to the % identity to carboxypeptidase B mutant, a sequence search revealed that SEQ ID NO 4 also has 39.6 % identity to bovine carboxypeptidase B (cleaves basic amino acids) as well as 38.1% identity to mouse carboxypeptidase A (cleaves hydrophobic amino acids). Further, Reznik teaches that carboxypeptidases which have different functions, but belong to the same subfamily, only have about 50% homology to each other. Therefore, absent any evidence as to the actual function or activity of the polypeptide of SEQ ID NO 4, one skilled in the art would not know whether the

biochemical activity of the claimed subject matter would be the same as that of a similar known biomolecule.

Further, with regard to newly added claim 31, the claimed invention is also drawn to an isolated polypeptide comprising an amino acid sequence which is at least 99% identical to SEQ ID NOS 4 which broadly encompasses variants and mutants with altered or wildtype function or activity. It is known for nucleic acids as well as proteins, that even a single nucleotide or amino acid change or mutation can destroy the function of the biomolecule in many instances, albeit not in all cases. The effects of these changes are largely unpredictable as to which ones have a significant effect versus not. (See Proudfoot et al, J. Biol. Chem., vol. 271, pp. 2599-2603 which teaches that in recombinant human RANTAS, a single residue at the amino terminus of the molecule can change the activity of the polypeptide, see abstract. The specification does not teach the biological function or activity of SEQ ID NO 4. Although SEQ ID NO 4 shows homology to metallocarboxypeptidases of the digestive subgroup, the sequence search cited previously showed comparable homology to carboxypeptidase A and B, which have different substrates and therefore function differently, as noted earlier carboxypeptidase B cleaves basic amino acids and carboxypeptidase A cleaves hydrophobic amino acids. Therefore, the citation of sequence similarity results in an unpredictable and therefore unreliable correspondence between the claimed biomolecule and the indicated similar biomolecule and therefore lacks support regarding enablement. Since the specification has not demonstrated the function or biological activity of SEQ ID NO 4, and since the recitation of functionally different domains and the

disclosed sequence similarity provides an unpredictable and unreliable correspondence between the activity of SEQ ID NO 4 and similar biomolecules, the skilled artisan would be required to perform undue experimentation to make or use the claimed polypeptides. Without the recitation of functional language, the claim does not exclude allelic variants having a different functional activity from the encoded protein disclosed as SEQ ID NO 4, nor has the specification taught where to modify the polypeptide to produce a protein with at least 99% identity to SEQ ID NO 4 that has the same or altered biological activity or function. The skilled artisan would be required to perform manipulations and extensive modification of the protein to determine where and how to make modifications to determine which fragments of the polypeptide were responsible for it's activity. Due to the lack of guidance from the specification as to which parts of the claimed polypeptides correspond to active domains, these modifications and manipulations would require trial and error, which is considered undue experimentation. In addition, further experimentation would be required of the skilled artisan to determine a use for the polypeptides of the claimed invention.

Response to Arguments

The response traverses the 101 and 112/first paragraph (enablement) rejection. The response asserts that the specification states that SEQ ID NO 4 shares homology with carboxypeptidase B and that one of ordinary skill in the art accepts structural homology based on amino acid identity as a credible method of determining the function of a polypeptide. This argument has been thoroughly reviewed but was not found persuasive. The rejection made in the

previous office action did not question the credibility of the utility asserted in the specification, that SEQ ID NO 4 was a member of the metallocarboxypeptidase family. Further, the rejection did not question that based on the homology and Blast analysis in the specification, SEQ ID NO 4 was likely a member of the metallocarboxypeptidase family. The rejection did state that the specification's disclosure of a specific or substantial utility for the claimed polypeptide was unclear as the specification teaches both that SEQ ID NO 4 has putative carboxypeptidase A metalloprotease family signature domains and that SEQ ID NO 4 also has homology to carboxypeptidase B. Carboxypeptidase A and B, while being members of the digestive metallocarboxypeptidase family, have different specificities and functions (see p. 6, lines 6 and 7 of the previous office action). Carboxypeptidase A cleaves hydrophobic amino acids from the C-terminal end of a peptide while carboxypeptidase B cleaves basic amino acids. The rejection further stated that a sequence search of protein databases and SEQ ID NO 4 also showed comparable homology between SEQ ID NO 4 and both Carboxypeptidase A and B. Therefore, based on the specification's disclosure, as well a search of the protein database, the skilled artisan would not have known the specificity or specific function of the polypeptide of SEQ ID NO 4, that is, does it cleave basic or hydrophobic amino acids.

The response presents bioinformatics evidence in the form of a Clustal W analysis that demonstrates that SEQ ID NO 4 is a digestive metallocarboxypeptidase because it 1) exhibits homology above the expected average for subfamily members, 2) it contains all the signature domains and conserved amino acid residues, and 3) it does not contain a transthyretin-like

folding domain present in all metallocarboxypeptidase regulatory family members. The bioinformatic evidence presented in the response was thoroughly reviewed, however such evidence was not found persuasive. Firstly, the bioinformatics analysis does not make clear to the skilled artisan what the specificity and specific function of SEQ ID NO 4 because this analysis, as well as that presented in the specification and the prior art in general does not teach whether SEQ ID NO 4 cleaves basic or hydrophobic amino acids, that is does it function like carboxypeptidase B or carboxypeptidase A. Such teaching is critical for the skilled artisan to determine what the specificity and specific function of SEQ ID NO 4 is. Secondly, the bioinformatics evidence is not supported by the actual experimental evidence set forth in the response. The response also asserts that preliminary experiments carried out using supernatant containing the polypeptide of SEQ ID NO 4 were inconclusive and that no statistically significant activity was observed on the substrates hippuryl-Arginine and hippuryl-Leucine-phenylalanine. This evidence was thoroughly reviewed but was not persuasive in overcoming the rejection because the experimental evidence set forth in the response does not support the bioinformatics evidence in the response or the Blast and homology analysis in the specification. While homology and bioinformatics analysis suggests that SEQ ID NO 4 is a member of the digestive metallocarboxypeptidase family, the actual experimental evidence set forth in the response does not support such function. Based on the experimental evidence set forth in applicants response, the skilled artisan would not be able to determine whether SEQ ID NO 4 has activity as a digestive metallocarboxypeptidase nor what the specificity or specific function of SEQ ID NO 4

is, without further experimentation. It is further noted that the results of such experimentation would be unpredictable as the response teaches that no statistically significant activity was observed with either hippuryl-Arginine or hippuryl-Leucine-phenylalanine as substrates.

Written Description

6. Newly added claim 31 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claim is drawn to a polypeptide sequence which is 99% identical to the amino acid of SEQ ID NO 4. Such recitation, however, encompasses mutants and variants of SEQ ID NO 4 with or without altered function. The specification, however, does not teach the specificity or specific function of SEQ ID NO 4, nor does the specification teach which amino acids can be altered such that the function of SEQ ID NO 4 are altered or remain intact. The specification only teaches that SEQ ID NO 4 has homology to metallocarboxypeptidases, more specifically that SEQ ID NO 4 has metallocarboxypeptidase A signature domains and homology to carboxypeptidase B, however such homology analysis does not make clear the specificity or specific function of SEQ ID NO 4 because carboxypeptidase A cleaves hydrophobic amino acids while carboxypeptidase B cleaves basic amino acids. The recitation of the polypeptide of SEQ ID NO 4 is therefore not representative of the functionally different proteins from this broad class

of claimed polypeptides, nor do the teachings in the specification make clear to the skilled artisan which amino acids can be changed to result in a protein with similar or altered activity as the polypeptide of SEQ ID NO 4.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

With the exception of SEQ ID NOS:4 , the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides and/or proteins, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993), and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966.

An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. Fiers v. Revel, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id. at 1170, 25 USPQ2d at 1606.

Accordingly, the specification does not provide an adequate written description of the invention of claim 31.

Conclusion

7. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however,

will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

8. No claims are allowable.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jehanne Souaya whose telephone number is (703)308-6565. The examiner can normally be reached Monday-Friday from 9:00 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax phone number for this Group is (703) 305-3014.

Any inquiry of a general nature should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Jehanne Souaya

Jehanne Souaya
Patent examiner
Art Unit 1634
October 18, 2002

W. Gary Jones
Supervisory Patent Examiner
Technology Center 1600